

**REMARKS**

Claims 1, 4-10, 16-17, 19-20, 23-26, 31-35, 39-41, and 71-72 are currently pending in the above-referenced application. Claims 2-3, 11-15, 18, 21-22, 27-30, 36-38, and 42-70 have been cancelled. Applicant reserves the right to prosecute the subject matter of the cancelled claims in one or more continuation or continuation-in-part applications. Claims 1, 25, 40, and 71 have been amended to further describe the invention.

**Claims Are Patentable Pursuant to 35 U.S.C. § 103(a)**

Claims 1, 4-10, 16, 17, 19, 20, 23-26, 31-35, 39-41, 71, and 72 have been rejected under 35 U.S.C. § 103(a) as unpatentable over Pennanen et al. ("Effect of Liposomal and Free Bisphosphonates on the IL-1 $\beta$ , IL-6, and TNF- $\alpha$  Secretion from RAW 264 Cells In Vitro," *Pharmaceutical Research*, Vol. 12, No. 6, pp. 916-922, 1995) and Hack, et al. (U.S. Patent No. 6,090,777) in view of Ylitalo ("Bisphosphonates and Atherosclerosis," *Gen. Pharmacology*, Vol. 35, pp. 287-296, 2002) and Hope, et al. (U.S. Patent No. 6,139,871). Applicants respectfully disagree with this rejection.

As recognized by the Examiner in the pending Action, the rejection is premised on a basic disagreement over the claim term "having." The Examiner prefers the term "during" while applicants prefer the term "having" – both terms expressing the concept that the patient is "undergoing" or "experiencing" an acute myocardial infarction – as the previously submitted definition of "having" indicates. The terms "having" and "during" are both present tense terms. According to Webster's Ninth New Collegiate Dictionary, a present participle is a "participle that typically expresses present action in relation to

the time expressed by the finite verb in its clause and that in English is formed with the suffix -ing." (See Merriam-Webster's Ninth New Collegiate Dictionary, Merriam-Webster, Inc., Springfield, MA, p. 931 (1985) (submitted herein).) It is therefore reasonable to assume that a general understanding of the terms "having" and "during" are words that express present action. Moreover, the phrases "having a myocardial infarction" and "during a myocardial infarction" are not instant events but indicate a period of time where a patient is undergoing the ischemic and reperfusion events that constitute a myocardial infarction and cause damage to the myocardium. The claimed formulation is administered to a patient during this period of time. In any case, to further the prosecution of this application and facilitate allowance, applicants have amended claims 1, 25, 40, and 71 to recite that the patient is treated "during" an acute myocardial infarction ("AMI"). Applicants respectfully request reconsideration of the pending claims in view of this new claim language.

As presented in detail in the Response filed on June 30, 2010, the pending rejection relies on three references, each of which describes treating chronic diseases: *i.e.*, Pennanen, Hope, and Ylitalo. The skilled person would not look to a treatment for a chronic disease for guidance in finding treatments for acute diseases. Acute diseases require quick and sometimes extreme treatments in contrast with chronic diseases which must be tolerated over long periods of time. Applicants believe that the instant claims are patentable over the cited prior art.

Further, as explained in the responses submitted on November 10, 2009 and June 30, 2010, one skilled in the art would not combine Pennanen, Ylitalo or Hope with the Hack reference because, it was understood in the art at the time of the invention

that liposomes, such as those allegedly described in Pennanen, Hope and Ylitalo, would activate the complement system, as evidenced, for example, by the article by Szebeni. (See Janos Szebeni, "The Interaction of Liposomes with the Complement System," *Critical Reviews in Therapeutic Drug Carrier Systems*, 15(1):57-88 (1995), submitted with June 30, 2010 Response.) As previously pointed out, the Szebeni article provides an overall review of the state of the art on liposome-induced activation of the complement system and details studies with both haptenized liposomes **and non-haptenized liposomes**. *Inter alia*, the Szebeni article contains a summary of a study by Wassef that demonstrates that the i.v. injection of **non-haptenized** liposomes elicit a natural antibody-mediated **activation** of the complement system thereby activating complement just as haptenized liposomes do. (See Szebeni, pp. 61 and 67.) The liposomes used by Wassef contained only DMPC, DMPG, and cholesterol, and therefore were non-haptenized. (See Szebeni, pp. 61 and 67.) Moreover, Szebeni concludes that plain, phospholipid/cholesterol vehicles were shown recently to be effective C activators without special antigen, hapten, or added antibody. (See Szebeni, p. 73.) Thus, the teachings of Szebeni are instructive of the state of the art regarding complement **activation** by haptenized **and non-haptenized** liposomes at the time of the invention, demonstrating the skilled artisan would not have used the Hack teaching of treating an AMI by inhibiting complement to reach an invention involving treating an AMI using liposomes (of any kind) because Szebeni teaches such liposomes will **activate** complement and not inhibit it.

Hack is inconsistent with the claimed invention in yet another aspect. Hack requires the use of a naked C-1 esterase inhibitor, *i.e.*, an inhibitor that is not

encapsulated in a liposome. However, the claimed liposomal encapsulation would completely incapacitate the inhibitor's ability to bind to its requisite binding partner by concealing the inhibitor binding site inside a liposome. (See Markovic, et al., "Acquired C1 Esterase Inhibitor Deficiency," *Ann. Intern. Med.*, 132:144-150, 144 (2000).) In fact, the inhibitor liposome would have the opposite effect, according to Szebani and result in complement activation. For this additional reason, the claims are patentable over the cited art.

### **Double Patenting Rejection**

MPEP 804 states that if "a 'provisional' nonstatutory obviousness-type double patenting (ODP) rejection is the only rejection remaining in the earlier filed of the two pending applications, while the later-filed application is rejectable on other grounds, the examiner should withdraw that rejection and permit the earlier-filed application to issue as a patent without a terminal disclaimer." The allegedly conflicting claims (i.e., claims 1-12 of copending Application No. 10/871,488 and claims 1, 4-10, 17-20, 23, 24, 27-29, 32-36, 38 and 41 of copending Application No. 11/190,787) are currently undergoing prosecution and have not been allowed. Applicants respectfully assert that the above arguments have overcome the pending 103 rejection. Therefore applicants respectfully request this rejection be withdrawn and the pending claims of the instant application be allowed. Reconsideration and withdrawal of these rejections is respectfully requested.

### **CONCLUSION**

Based on the foregoing remarks, applicants respectfully request reconsideration and allowance of this application over the Non-Final Office Action of August 25, 2010.

If any issues remain, or if the Examiner has any suggestions for expediting allowance of the application, the Examiner is invited to contact the undersigned attorney.


#### AUTHORIZATION

The Commissioner is hereby authorized to charge any additional fees which may be required for consideration of this Pre-Appeal Brief to Deposit Account No. 50-4387, Order No. 92114.005US1.

In the event that an extension of time is required, or which may be required in addition to that requested in a petition for an extension of time, the Commissioner is requested to grant a petition for that extension of time which is required to make this response timely and is hereby authorized to charge any fee for such an extension of time or credit any overpayment for an extension of time to Deposit Account No. 50-4387, Order No. 92114.005US1.

Respectfully submitted,  
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